Normal Kidney

Introduction

This lesson combines **where things are** (anatomy) with **what things look like** (histology). It sets the stage for the physiology lessons that follow. If this is the first time you've encountered the kidneys in medical school, this will serve as an orientation. If it's not the first time you've encountered the kidneys, try to forget everything you've learned, or this may be an uncomfortable ride.

We also do things in nephrology that other texts don't. Nephrology is generally considered the most difficult organ system in medical school. We employ some unorthodox strategies that may feel foreign or that are not used anywhere else. We promise: the way to learn the kidney is the way we teach it. This lesson serves only as the What. The How, Why, and mechanisms will be revealed as we progress. You won't get a profound understanding of how the kidney works from this lesson, but you will get the necessary facts to move forward. Don't try to figure things out or commit to memory the details in this lesson. Instead, accept the information as accurate, and in subsequent lessons we'll justify the information with details about each thing.

Anatomy: Location in the Abdomen

The kidneys sit under the liver on the right and under the spleen on the left. The kidneys are **retroperitoneal**. Where the peritoneum comes into contact with the capsule of the kidney, it is called visceral peritoneum. The kidneys are protected by the rib cage. Because the liver is on the right and is bigger than the spleen, the right kidney is slightly lower (L1–L4) than the left kidney (T12–L3). Because the liver is bigger than the spleen, during embryonic development the liver impinges on the development of the right kidney, so the right kidney is smaller than the left.

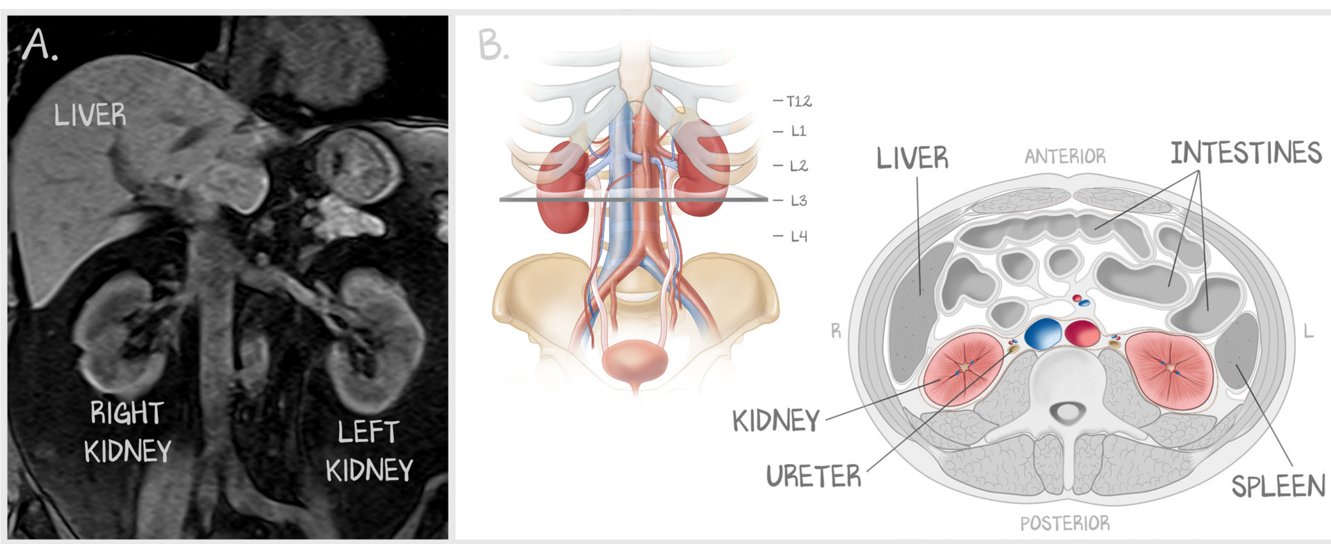

Figure 1.1: Kidney Anatomy
(a) Normal anatomic location of the kidneys and ureters as seen on radiographic imaging. (b) Gross illustration demonstrating the position of the kidneys relative to the peritoneal cavity below the level of the liver and other abdominal structures as seen on a sagittal CT.

The ureter, artery, and vein connect to the kidney through a central region called the **hilum**. The ureter is the most posterior—posterior to the artery, posterior to the vein. The ureter connects the kidney to the bladder, constantly draining any urine made by the kidney into the bladder. The ureter exits the kidney at

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the **ureteropelvic junction** (the renal pelvis is the last structure in the kidney's collecting system and the funnel-like mouth of the ureter). The ureter then descends, passes over the **psoas muscle**, and connects with the bladder. The path and appearance of the ureter are similar to those of the cardinal ligament of the uterus, so care must be made when performing uterine surgery not to mistake the ligament (which should be cut) for the ureter (which definitely should not be cut).

Anatomy: Gross Anatomy of the Kidney

The kidney can be divided into three anatomical regions: the cortex, medulla, and pelvis. The kidney can be divided into two functional regions: the urinary generation system and the urinary drainage system. The cortex and medulla contribute to the urinary generation system. The medulla and pelvis contribute to the urinary drainage system. These statements may seem foreign and uncomfortable right now. The next paragraph is to help you orient the overall structure of the kidney, helping you categorize anatomy and function from the beginning. Read through once, look at Figure 1.2, then come back and read this section again.

Embryonically, the urinary generation system is derived from the metanephric mesenchyme. That thing becomes the nephrons—glomeruli, convoluted tubules (proximal and distal), and the loop of Henle (thin descending and thick ascending). Nephrons are mostly in the cortex, except for the loops of Henle, which contribute to the medullary pyramids. Embryonically, the urinary drainage system is derived from the ureteric bud. That thing becomes the ureters, pelvis, and calyces, and contributes the collecting ducts to the renal pyramids.

So there is a urinary generation system and a urinary drainage system. The difficulty is that there are three layers of the kidney that comprise two systems. Which means overlap. Orient yourself like this—a capsule surrounds the kidney. The outermost layer of the kidney, the one just under the capsule, is the cortex. Cortex deals only with urinary generation. The innermost layer of the kidney, the one at the hilum, is the pelvis. The pelvis deals only with urinary drainage. The middle layer, the layer between the cortex and the pelvis, is the medulla. The medulla is made of the urinary generation system and the urinary drainage system. This organization of the kidney may not be familiar, but it is the way you should start thinking of the kidney. Let's explore the details of the gross anatomy of each layer.

The **renal pelvis** is the innermost portion of the kidney. The actual pelvis represents the most dilated portion of the ureter. But we want you seeing the pelvis layer (an OME term) as everything from minor calyx to ureter. Urinary drainage begins with the collecting ducts of the medulla, which coalesce into the **minor calyces**. The minor calyces combine into **major calyces**. The final collection of all calyces is at the renal pelvis—the exit of all common tributaries of urine drainage, which is carried to the bladder by the ureter.

The **renal medulla** is the middle layer of the kidney between the pelvis and cortex. The medulla is formed by medullary pyramids and the renal columns. The **renal columns** share an embryonic origin with the cortex. Through the renal columns medium-sized blood vessels run from the hilum to the cortex. The renal columns exist between the pyramids. The **medullary pyramids** are comprised of the straight tubules—the loops of Henle and the collecting ducts, giving the impression that they are streaked, called medullary rays. The apex of the pyramid directs urine flow toward minor calyces, toward the pelvis. The base of the pyramid touches the cortex. Medullary pyramids share an embryonic origin with both the cortex (the loops of Henle) and the pelvis (the collecting ducts).

The **renal cortex** is the outer layer of the kidney, between the medulla and capsule. The cortex has a smooth, dark exterior. It is where the **glomeruli** and **convoluted tubules** are. It is where the smallest named arteries go. From the cortex, the vessels dive into the medulla (vasa recta), and will return to the cortex before becoming veins to exit the kidney.

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The kidney is surrounded by a **capsule**. The capsule is a membranous sheath, opening only at the hilum to let the vessels out. The capsule is thin, but keeps the organ's bits together in trauma, and also acts as a layer of protection from penetrating trauma or infections.

The kidney is said to have poles. The **upper pole** is the top of the kidney, if a person were standing up. The **lower pole** is toward the feet. Pole just means some laterality, and people may say "urinary pole" to mean "toward the renal pelvis."

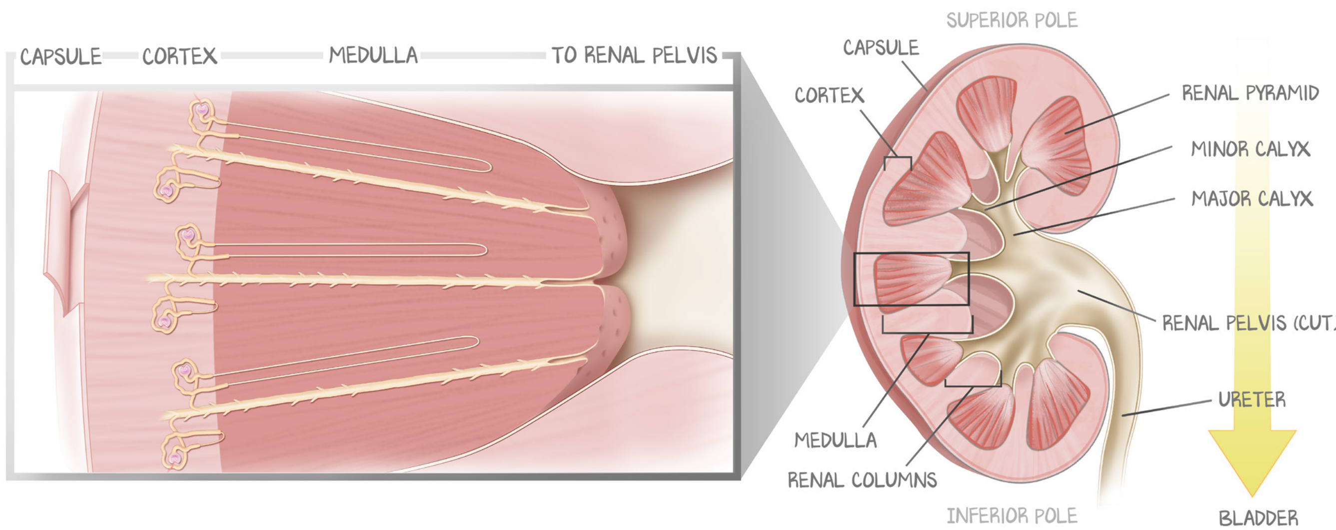

Figure 1.2: Functional Layers of the Kidney
We want you thinking in these terms: there are three layers to the kidney. Three. The pelvis, the medulla, and the cortex. The whole thing is surrounded by a capsule. The urinary pelvis collects the output of the calyces and feeds the ureter. The pelvis is the innermost layer of the kidney and is comprised only of urinary drainage tissue. The cortex is the outermost layer of the kidney. It contains the glomeruli and convoluted tubules. The renal medulla is comprised of renal columns, and the renal pyramids are comprised of the straight tubules.

Anatomy: Gross Vasculature of the Kidney

The left renal artery originates directly from the aorta on the left and irrigates the left kidney. The right renal artery originates directly from the aorta on the right and irrigates the right kidney. The **renal arteries**, therefore, each originate from the aorta. From the renal arteries the adrenal arteries branch. The venous drainage is not so simple. The **right renal vein** (because it is close to the vena cava on the right side) connects directly to the IVC, while the **left renal vein** forms a common tributary with the adrenal vein and the vein of the gonads.

Each kidney has a single **renal artery** that enters at the hilum. The renal artery then splits into **segmental arteries**, traveling along major calyces. The segmental arteries then split to give rise to the **interlobar arteries** which traverse the renal columns between medullary pyramids. The interlobar arteries branch into **arcuate arteries** in the cortex. The arcuate arteries are the smallest named arteries in the kidney. From arcuate arteries branch small vessels that will become the glomerular capillaries and peritubular capillaries. The venous drainage comes from the cortex, **mirroring arterial distribution**, and exits through the hilum.

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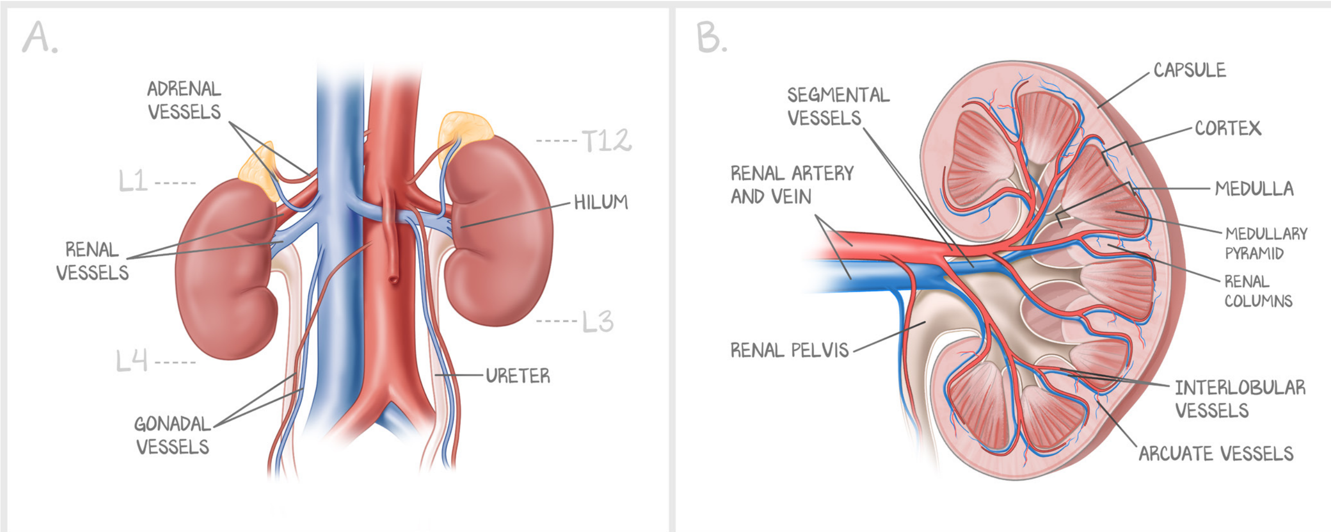

Figure 1.3: Renal Vasculature
(a) The kidney on the left, being on the opposite side of the body as the inferior vena cava, has a common drainage of the adrenal, gonadal, and renal vein before connecting to the inferior vena cava. The kidney on the right, being on the same side as the inferior vena cava, has an independent venous drainage from the adrenal and gonadal veins. (b) The renal artery gives rise to segmental arteries that follow major calyces, and interlobar arteries that follow minor calyces and ascend the renal columns, finally branching into arcuate arteries that penetrate the cortex.

Nephron Anatomy and Vasculature

The nephron is the **smallest functional unit** of the kidney. Every nephron is made of five segments—the **glomerulus**, the **proximal convoluted tubule** (PCT), two segments of a **loop of Henle** (thin descending limb and thick ascending limb), and a **distal convoluted tubule** (DCT). Every nephron connects its DCT into a **collecting duct** (CD). There is an abundance of **cortical nephrons**, which have only very small loops of Henle that do not project into the medulla. They are used to filter toxins and regulate electrolytes. There are also **juxtamedullary nephrons** that project their loop of Henle tubules deep into the medulla. All nephrons share the same cortical components. All nephrons have loops of Henle. The cortical nephrons have shallow loops, while the juxtamedullary nephrons have very deep loops. These deep projections allow the establishment of concentration gradients so that all nephrons can regulate ions and water.

In the **cortex** is where the glomerulus, proximal convoluted tubule, and distal convoluted tubule of every nephron are. In the **medulla**, specifically the medullary pyramids, is where the loops of Henle and the collecting ducts are. The loops of Henle and collecting ducts are not convoluted tubules, and are instead termed straight tubules. The pyramids appear to be marked with straight lines on gross inspection. These straight lines, seen with the naked eye, are called **medullary rays**. These straight lines are created by the conglomeration of the microscopic straight tubules. The nephron ends at the collecting duct. The nephron is derived from the metanephric mesenchyme, from the cortex, and is the urinary <u>generation</u> system. The collecting duct is from the ureteric bud, of the urinary <u>drainage</u> system.

The arcuate arteries are in the cortex. From these small arteries the microscopic vasculature of the nephron arises. This vasculature consists of two functionally distinct units—the blood vessels of filtration and the blood vessels of oxygenation (the vasa recta). The kidney is unique in that there are two arterioles and two capillary beds. These arterioles are in series, one after the other. The first capillary bed is within the glomerulus, between the two arterioles, and is not where oxygen is extracted but rather where blood is filtered. These are called the **glomerular capillaries** and are the **capillaries of filtration**. The second capillary bed is alongside the cells of the tubules, and these are just like every capillary everywhere else in the body. These capillaries are where red blood cells oxygenate tubular cells. They are called the **peritubular capillaries** and are the **capillaries of oxygenation**.

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Blood enters the glomerulus through the **afferent arteriole**, then passes through the **glomerular capillaries** and through the **efferent arteriole**. The efferent arteriole gives rise to the **vasa recta**. The vasa recta takes the shape of the loop of Henle that it supplies. From the arterial side of the vasa recta, **peritubular capillaries** form. Those peritubular capillaries join the venous side of the vasa recta and ascend toward the cortex. Vasa recta venules coalesce to form the arcuate vein.

We explore and compare the details of the urinary generation and urinary drainage systems in detail in Kidney #2: *Kidney Embryology*. We explore the details of the glomerular capillary in Kidney #3: *Glomerular Filtration*. We explore the details of loop of Henle and the vasa recta, and their significance, in Kidney #4: *Regional Transport and Regional Pharmacology* and Kidney #5: *Water*. It's okay if it feels overwhelming right now. We've got four more lessons to hash out the details.

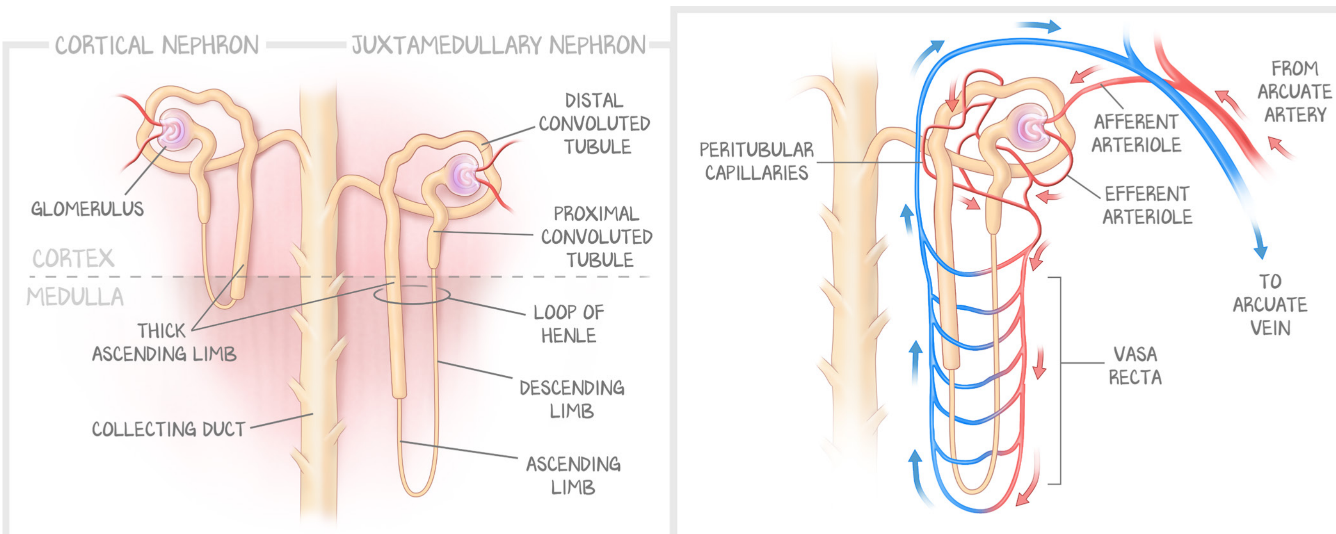

Figure 1.4: Nephron Anatomy
All nephrons consist of five segments: glomerulus, proximal convoluted tubule, thin descending limb of the loop of Henle, thick ascending limb of the loop of Henle, and distal convoluted tubule. A juxtamedullary nephron penetrates its loop of Henle deep into the medulla. A cortical nephron has only a shallow projection. The vasa recta, the penetrating capillary bed that feeds the tubule cells in the medulla, has the same shape as the loop of Henle it feeds.

The Glomerular Structures

Filtration occurs at the glomerulus. Filtration forces are discussed in Kidney #3: *Glomerular Filtration*, and how filtration works is discussed in Injury #2: *Tubulointerstitial Diseases*. This section is meant only as an orientation to what the structures of the glomerulus are and what they look like, not what they do.

The glomerulus is a combination of Bowman's capsule, the glomerular capillary, and the cells in between. The afferent arteriole brings blood into the glomerulus. From the afferent arteriole the glomerular capillaries are formed. The lining of the glomerular capillary, identical to every capillary everywhere else, is lined by endothelium—one-cell thick. Endothelial cells sit on a basement membrane. That basement membrane is shared by the lining of the Bowman's space—the epithelium of Bowman's space. This epithelium is also one cell thick. Bowman's space is where the initial filtrate is formed, the fluid pushed out of the glomerular capillary. Where the epithelium of Bowman's space touches a glomerular capillary, where it shares the basement membrane with an endothelial cell, that epithelium is termed the visceral epithelium. The cells of the visceral epithelium differentiate into a specialized type of cell, found nowhere else in the body, and are termed podocytes. Where the epithelium of Bowman's space does not touch a glomerular capillary remains normal epithelium and is referred to as parietal epithelium. The

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epithelium of Bowman's space is continuous. The **renal corpuscle** is a spherical structure that contains Bowman's space, the glomerular capillaries, and the glomerular mesangial cells. We've chosen to call that thing the glomerulus, and the capillaries themselves glomerular capillaries.

Immediately adjacent to the glomerulus (renal corpuscle) is the juxtaglomerular (JG) apparatus, the afferent arteriole, and the efferent arteriole. The glomerulus filters urine. The JG apparatus has a vital role in filtration. We cannot discuss one without the other. And because they are histologically next to each other, you will be able to see them both on a slide. So we include the glomerular structures (endothelium, basement membrane, epithelium of Bowman's space) in the discussion with the extraglomerular structures that matter to the glomerulus (afferent arteriole, efferent arteriole, JG apparatus). Let's go through each one in detail.

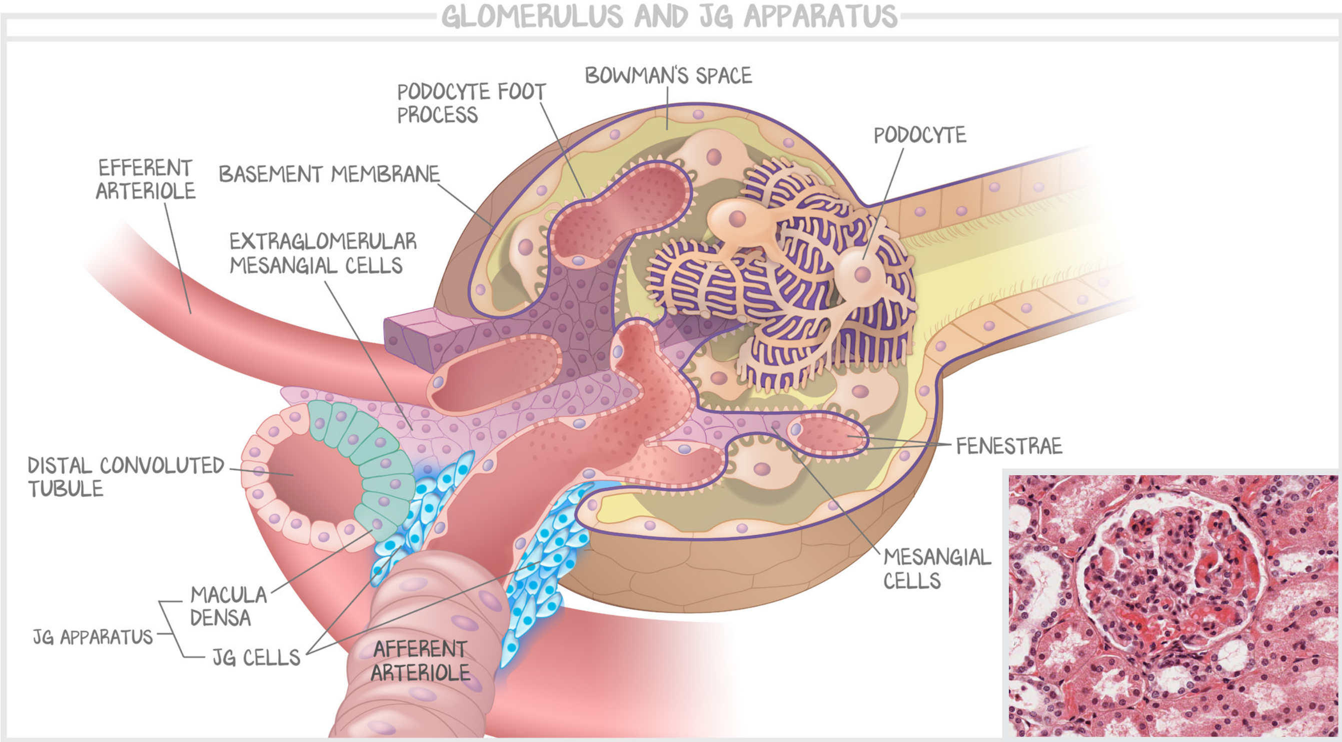

Figure 1.5: Glomerulus and Juxtaglomerular Apparatus

Capillary endothelium. An arteriole gives rise to a capillary bed, a network of capillaries. Those capillaries are lined by an epithelium. The single-cell-thick squamous epithelium of the capillary is called an **endothelium**, just like every other blood vessel. The difference is that the endothelium of the glomerular capillary is **highly fenestrated** (gaps that are 70–90 nm in size). Fenestrations are tiny portals where proteins, water, and ions can easily diffuse to the basement membrane. Highly fenestrated means there are a lot of fenestrations, as shown in Figure 1.6.

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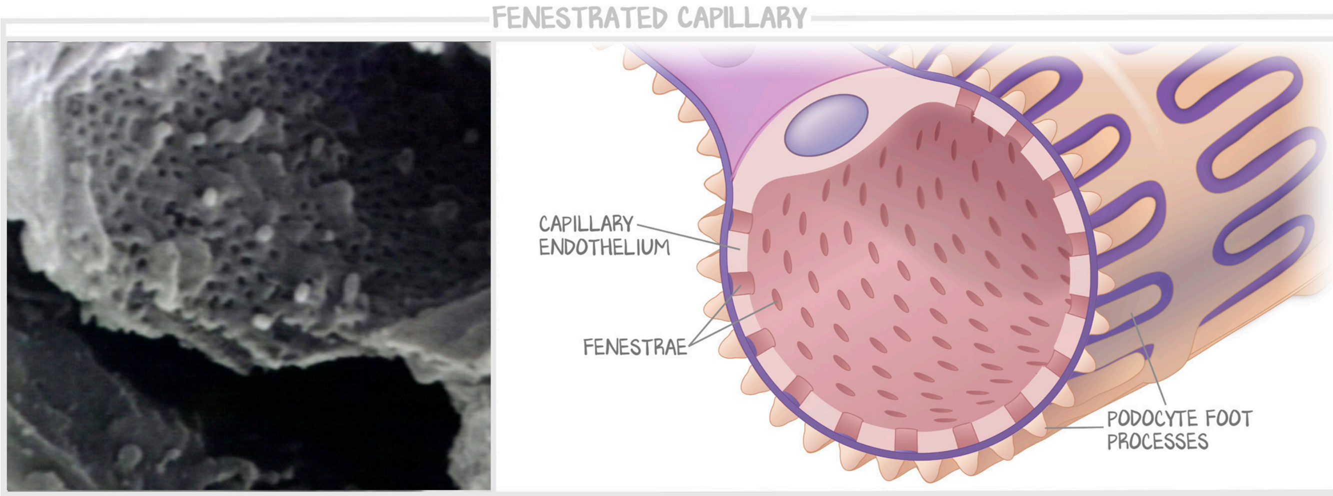

Figure 1.6: Fenestrated Capillaries

Podocytes. The epithelium in contact with the capillary undergoes differentiation into **podocytes**. Podocytes are the epithelial lining of Bowman's capsule, but look and act differently than the parietal layer epithelium. The podocyte body, where the nucleus and organelles are, float in the urinary space. Podocytes project primary processes from their cell bodies. Primary processes then project smaller secondary processes that wrap around the that wrap around the endothelium on the outside of the capillary. From these secondary projections project even smaller **pedicles** (foot processes). The pedicles interdigitate with each other.

Basement membrane. Between the podocytes and the capillary endothelium is the **glomerular basement membrane**. The basement membrane is filled with collagen and negatively charged proteins. Like every basement membrane, it is made of type IV collagen (lamina densa, "of the cell," from General Physiology #9: *Epithelium*) and proteins of the extracellular matrix such as elastin and fibrillin. Podocytes and endothelial cells share the same basement membrane. The only other location where an endothelial cell shares a basement membrane with another cell is in the lungs, a fact that explains certain autoimmune conditions we'll study later.

Mesangial cells. The support structure for the glomerular capillary is the **mesangial cells**. These cells exist between endothelial cells and the tubule cells (discussed next) within the glomerulus. Mesangial cells provide **structural support**, secrete prostaglandins, and are involved in **phagocytosis**. They keep the filtration slits clean and will proliferate in disease where protein complexes deposit. They do not play a direct role in filtration, but are part of the renal corpuscle.

Juxtaglomerular apparatus. The JG apparatus consists of the juxtaglomerular cells (JG cells), the macula densa, and extraglomerular mesangial cells. The **extraglomerular mesangial cells** (by the way, these aren't called extracorpuscular, which is why we only mentioned the corpuscle once) are a just a continuation of the glomerular mesangial cells. The division between extraglomerular and glomerular is rather arbitrary, as the extraglomerular mesangial cells serve the same purpose—structural support—as the glomerular mesangial cells. The **macula densa** is a specialized region of tubular epithelium at the level of the glomerulus, where the nephron tubule changes from the thick ascending limb of the loop of Henle to the distal convoluted tubule. The macula densa is the lining of the tubule. The macula densa senses flow passing through the tubules. effectively monitoring glomerular filtration rate. The macula densa monitors flow and informs the JG cells what to do. The **JG cells** are highly specialized cells that live only very near to the afferent arteriole. The JG cells are the output of the JG apparatus. The JG

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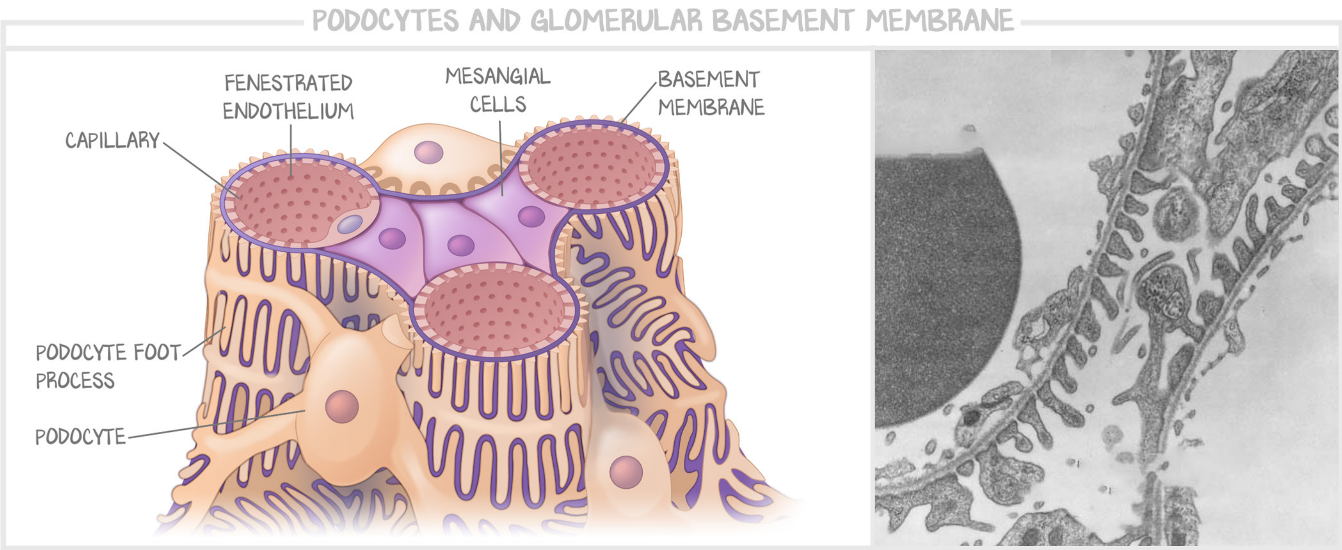
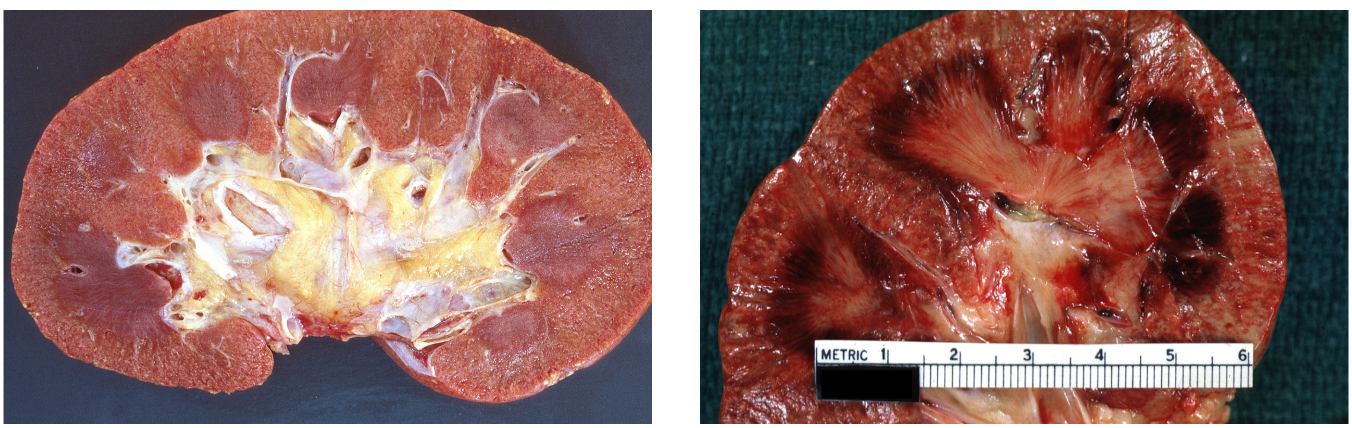
apparatus influences the local effects of the nephron it is a part of by affecting the afferent arteriole. The JG apparatus also influences all arterioles throughout the body by releasing renin. The details of how are discussed in Kidney #3: *Glomerular Filtration*).



(a) **(b)**

Figure 1.7: Podocytes and Glomerular Basement Membrane
(a) Each capillary bed is tortuous, a bundled-up network of capillaries twisting and turning. (b) The glomerular basement membrane (GBM) is the continuous grey bands between the foot processes of podocytes and the endothelial cell. At this magnification, the space between podocyte foot processes makes the endothelial cell appear discontinuous. These are fenestrations.



(a) **(b)**

Figure 1.8: Real Normal Kidneys
(a) Normal kidney demonstrating the three layers—cortex, medulla, pelvis—well. (b) Normal kidney demonstrating the medullary pyramids with their streaked rays clearly separated from the renal columns that have the consistency of the cortex.

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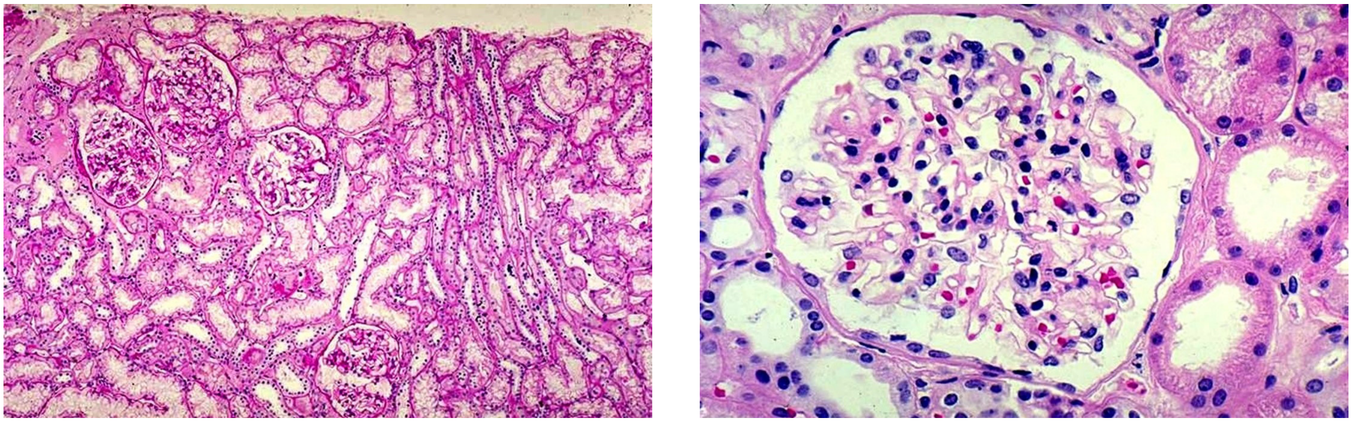

(a) (b)

Figure 1.9: Normal Kidney Histology
(a) Low-powered light microscopy of a PASH stain showing preserved glomeruli, tubules, and interstitium. (b) High-powered light micrscopy of a glomerulus. Notice the normal cellularity and thickness of the GBM.